Overview of Osteopetrosis

Osteopetrosis is a rare disorder that causes bones to grow abnormally and become overly dense. When bones become overly dense, they are brittle and can fracture (break) easily. In addition, bones may be misshapen and large, causing other problems in the body. For example, changes to the bone size and density of the skull can cause pressure on nerves leading to vision loss, hearing loss, and paralysis of the facial muscles.

As bone increases in size, the amount of space for the bone marrow (soft, sponge-like tissue in the center of most bones that produces blood cells) becomes crowded. Decreases in the amount of space for bone marrow can lead to low levels of cells in the body that fight infection, carry oxygen to the body's cells, or control bleeding.

Osteopetrosis is a genetic disease that a child inherits from their parents. The disorder may be mild to severe, and symptoms may appear early in infancy or later in adulthood. The treatment options depend on the type of osteopetrosis the person has.

What happens in osteopetrosis?

Normally, old bone is broken down and new bone is formed. However, this process does not work properly in people with osteopetrosis. Instead, old bone is *not* broken down as new bone is formed. This causes the bone to develop incorrectly, leading to dense, thick bones that can fracture easily.

Who Gets Osteopetrosis?

People with a family history of the disease are at greater risk of inheriting it through an abnormal gene that is passed on from one or both parents.

Types of Osteopetrosis

The types of osteopetrosis are broken into categories based on inheritance pattern, age the disease develops, and the severity of the disease. The types include:

- Autosomal recessive osteopetrosis is the severe infantile form of the disorder. The symptoms of this type develop at or shortly after birth and shorten life expectancy.

- Autosomal dominant osteopetrosis is the noninfantile form of the disorder and is also known as Albers-Schönberg disease. The symptoms of this type develop later than the infantile form and have a wide range of disease severity. Even within the same family, some people have little or no impact from the disease, while others are severely affected by the disease and have significant disability and shortened life expectancy. People with this type of osteopetrosis may not be diagnosed until adolescence or adulthood.
- X-linked osteopetrosis is a rare form of the disease and can affect many areas of the body.

Symptoms of Osteopetrosis

The severity of symptoms can vary depending on the type of osteopetrosis. They include:

- Bone fractures from brittle, dense bones.
- Nasal congestion from narrowing sinus cavities.
- Vision and hearing changes from enlarged bones pressing on nerves.
- Dental problems due to bone changes in the skull and jaw and because teeth come in later than normal.
- Low blood cell levels due to smaller amounts of bone marrow because of crowding in the center of bones can lead to anemia and infection.
- Infections in the bone (osteomyelitis).
- Chronic bone pain.

Cause of Osteopetrosis

Osteopetrosis is a genetic disease that, in most cases, a child inherits from one or both parents. Genes carry information that determines which features are passed to you from your parents. We have two copies of most of our genes, one from each parent.

People with osteopetrosis have a gene that causes the body to make too few or abnormal cells called osteoclasts. When the osteoclasts are missing, old bone is not broken down as new bone is made, leading to dense, weak bones.

The inheritance patterns help determine the type of osteopetrosis the person has.

- Autosomal recessive inheritance pattern happens when the parents each carry one copy of the mutated (changed) gene but do not show any signs or symptoms of the disease. It’s important to note that the mutated gene may not be passed from both parents to every child. Some children will not have any copies of the gene, and others may only have one copy, making them a carrier.

- Autosomal dominant inheritance pattern happens when only one mutated copy of the gene appears. This happens when the child inherits one copy of a mutated gene from one parent; however, sometimes the mutated gene appears with no family history.
- X-linked inheritance pattern causes a rare form of the disease and happens when a mutation occurs in genes on the X chromosome, one of the two sex chromosomes in each cell. This type of osteopetrosis usually affects boys.

Diagnosis of Osteopetrosis

Doctors diagnose osteopetrosis by:

- Taking a family and medical history.
- Performing an exam.
- Ordering laboratory tests and imaging studies.

Your doctor may order one or more of the following tests to diagnose osteopetrosis:

- X-rays to evaluate bone structure, including dense and misshapen bones.
- Genetic testing to help determine the specific cause and type of osteopetrosis.
- Blood tests to check:
  - Blood cell counts.
  - Vitamin and mineral levels.
  - Certain hormone levels.
- Computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) to evaluate changes in bone marrow space and skull.

Treatment of Osteopetrosis

Knowing the type of osteopetrosis helps doctors treat the symptoms and problems from the disease. Genetic testing allows doctors to examine specific changes in the genes so treatment can be tailored depending on the cause and expected severity of the disease. Treatments can include:

- Interferon gamma-1b is an injected drug designed to delay disease progression and is the only therapy specifically approved by the U.S. Food and Drug Administration (FDA) for the severe infantile form of the disease. It is not currently approved for the treatment of the noninfantile form of osteopetrosis.
- Corticosteroids may help improve some blood cell levels. Because they are potent drugs, your doctor will prescribe the lowest dose possible to achieve the desired benefit.
- Physical and occupational therapy can help children develop motor and other skills.

- Bone care may include casts, splints, or surgery to correct fractures and misshapen bones.
- Bone marrow transplant may be recommended for infants with the severe form of the disease and for people with bone marrow failure. Doctors will recommend this type of treatment on a case-by-case basis after reviewing the risks and benefits. Bone marrow transplant can cure the disease for certain people, but it cannot reverse damage that has already occurred.

Regular visits with the doctor are important to check symptoms and laboratory testing results, and to discuss potential treatments.

Who Treats Osteopetrosis?

Several different types of doctors diagnose and treat osteopetrosis. Often, people work with a team of doctors to provide the best treatment. These doctors may include:

- Endocrinologists, who treat hormonal and metabolic disorders.
- Dentists, who can help prevent dental problems and treat issues, including orthodontists and oral-maxillofacial surgeons.
- Geneticists, who study genes, especially how they are inherited and mutate.
- Hematologists, who specialize in blood disorders.
- Neurologists, who treat disorders and diseases of the spine, brain, and nerves.
- Neurosurgeons, who perform surgery for disorders and diseases of spine, brain, and nerves.
- Ophthalmologists, who treat disorders and diseases of the eye.
- Orthopaedists, who treat and perform surgery for bone and joint diseases.
- Otolaryngologists, who treat ear, nose, and throat disorders.

Living With Osteopetrosis

Living with osteopetrosis is different for each person. Some people have few or no symptoms, while others have many symptoms that affect their ability to perform daily activities. The following tips may help.

- See your health care providers on a regular basis.
- Talk to your doctor or physical therapist about which types of exercises are best for you based on the type of osteopetrosis you have.
- Ask your doctor about nutrition.
- Keep the lines of communication open. Ask family and friends for help when you need it.
- Reach out to online and community support groups.

Research Progress Related to Osteopetrosis

Research into causes and treatments of osteopetrosis continue to focus on:

- Genetic and molecular mechanisms of abnormal bone formation and breakdown.
- Gene therapy as a treatment for certain types of osteopetrosis.
- Development of medications to treat specific types of the disease.
- Surgical management of complications.
- Modifications to bone marrow transplantation that would decrease the risk of transplantation and make it a potential option for people with the noninfantile type of osteopetrosis.

Related Resources

U.S. Food and Drug Administration
Toll free: 888-INFO-FDA (888-463-6332)
Website: https://www.fda.gov

Drugs@FDA at https://www.accessdata.fda.gov/scripts/cder/daf/. Drugs@FDA is a searchable catalog of FDA-approved drug products.

Centers for Disease Control and Prevention, National Center for Health Statistics
Website: https://www.cdc.gov/nchs

NIH Osteoporosis and Related Bone Diseases ~ National Resource Center
Website: https://www.bones.nih.gov

Genetic and Rare Diseases Information Center
Website: https://rarediseases.info.nih.gov/GARD

Genetics Home Reference
Website: https://www.ghr.nlm.nih.gov/condition/osteopetrosis

American Academy of Orthopaedic Surgeons
Website: https://www.aaos.org

Orphanet
Website: https://www.orpha.net

If you need more information about available resources in your language or other languages, please visit our webpages below or contact the NIAMS Information Clearinghouse at

NIAMSInfo@mail.nih.gov.

- Asian Language Health Information
- Spanish Language Health Information